RESEARCH ARTICLE

Mucocutaneous manifestations of Chikungunya fever, an experience of tertiary care hospital

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Abstract

Objectives: To determine the frequencies of mucocutaneous manifestations of chikungunya fever, and to determine the association of positive serology with manifestations.

Method: The observational cross-sectional study was conducted at the Department of Dermatology, Jinnah Postgraduate Medical Centre, Karachi, from May 15, 2018, to January 15, 2019, and comprised patients who presented with early and late manifestations of chikungunya fever. Different cutaneous manifestations were confirmed by a consultant dermatologist. Data was analysed using SPSS 23.

Result: Of the 67 patients, 46(68.7%) were females and 21(31.3%) were males. The overall mean age was 30.24±7.89 years. Hyperpigmentation was the most frequent finding 31(46%), followed by maculopapular rashes and oral ulcers in 17(25%) each, and diffuse hair fall in 14(20%). There was no significant association between clinically suspected cases and serology-positive patients.

Conclusion: Chikungunya fever presented with unusual mucocutaneous findings, some of which remained present months or even years after the onset of chikungunya fever.

Keywords: Chikungunya fever, Maculopapular rash, Hyperpigmentation. (JPMA 71: 619; 2021)

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Introduction

Chikungunya fever (CF) is caused by Chikungunya virus with clinical triad of "fever, rash and arthralgia". Chikungunya virus, an Arbovirus belonging to the genus Alphavirus in the Togaviridae family, has a single-stranded ribonucleic acid (RNA) genome, a 60-70nm diameter capsid, and a phospholipid envelope.[1]

Previous outbreaks were reported between 1920 and 1950 in South Asia and in India during 2005.[2] Lately, Chikungunya outbreak started in November 2016 in Pakistan, infecting more than 30,000 residents of Karachi.[3]

For the first time Pakistan's Ministry of National Health Services, Regulations and Coordination stated cases of Chikungunya in the country in February, 2017 after 92 samples were sent to the National Institute of Health for testing, out of which 71 showed positive serology.[4]

A large variety of mucocutaneous manifestations have been documented in association with CF that has not been presented with other viral exanthems.[5] Several studies in India showed various cutaneous manifestation of CF.[1,2] But in Pakistan no study was done to identify mucocutaneous manifestations of CF. The current study was planned to determine the different frequencies of mucocutaneous manifestations of CF, and to determine the association of positive serology with manifestations.

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Patients and Methods

The observational cross-sectional study was conducted at the Department of Dermatology, Jinnah Postgraduate Medical Centre, Karachi, from May 15, 2018, to January 15, 2019. After getting approval from the institutional ethics review board, the sample size was calculated using the formula n= Z 2pq/ E2.[6] The sample was raised using purposive sampling technique.

Those included were patients who met the criteria of suspected CF. According to "case definition", "suspected cases" are those presenting with an acute illness characterised by the sudden onset of fever, with several symptoms, such as joint pain, headache, backache, photophobia and skin eruption during an epidemic of CF and in the absence of confirmatory serological tests.[5] Also included were patients who presented with skin manifestations and had a strong history of CF in preceding 2-3 years with documented evidence of positive serology. All patients with history of CF and early or late cutaneous manifestation were included. Patients having dengue fever were excluded.

All patients were examined and diagnosed by experienced consultant dermatologist after written informed consent was taken from the subjects for their images and other clinical information. These patients

either reported voluntarily because of skin lesions or were referred by medical departments.

Basic epidemiological data of the patients, including age and gender, was recorded. Clinical information of patients, such as disease manifestations and complications, was also collected. Chikungunya serology and complete blood count (CBC) was done subsequently. Based on all parameters, the disease was managed symptomatically and according to the latest guidelines.[1]

Data was analysed using SPSS 23. It was presented as mean ± standard deviation (SD), as well as frequencies and percentages. Chi square test and Fisher's Exact test were used for further analyses. $p<0.05$ was taken as significant.

Results

Of the 67 patients, 46(68.7%) were females and 21(31.3%) were males. The overall mean age was 30.24±7.89 years. Majority of the patients 59(88.01%) were aged 20-40 years. Immunoglobulin M (IgM) was positive in 40(59.7%) patients, and negative in 27(40.29%). The most common mucocutaneous finding was hyperpigmentation 31(46.3%); 10(14.92%) males and 21(31.34%) females. The

Figure-1: Hyperpigmentation at neck.

Table-1: Different Mucocutaneous Manifestations of chikungunya fever (CF).

S.No.	Features	CF Clinically Suspected* Patients, N=67	CF Serology Positive, N= 40	CF Serology Negative, N= 27	P Value
01	Hyperpigmentation	31 (46.3%)	18 (45.0%)	13(48.1%)	0.28
02	Maculopapular Eruption	17 (25.4%)	12 (30.0%)	5(18.5%)	0.80
04	Oral Ulcers	17 (25.4%)	10 (25.0%)	7(25.9%)	0.93
05	Diffuse Hair Fall	14 (20.9%)	10 (25.0%)	4(14.8%)	0.31
06	Lichenoid Eruption	11 (16.4%)	08 (20.0%)	3(11.1%)	0.33
07	Erythema of Pinna	04 (6.01%)	03 (7.5%)	1(3.7%)	0.64
08	Exacerbation of Psoriasis	03 (4.5%)	03 (7.5%)	0(0%)	0.26
09	Exacerbation of Acne	02 (3.0%)	02 (5.0%)	0(0%)	0.51

Table-2: Comparison with studies done in South Asia.

Variables	Our Study	Kumar et al[1]	Seetharam et al[21]	Riyaz et al[22]
Year/Place	2018-2019 /Karachi, Pakistan	2016 / Kota, India	2009-2010/Andhara Pardesh, India	2009/Calcit, Kerala
M:F Ratio	01:02.1	1.2:1	1.1:1	01:01.1
Hyperpigmentation	46.3% (Forhead, Nose, Mucosal, Dorsal Limbs And Joints)	39.2% (Nose, Face, Trunk, Mucosal)	51.9% (Diffuse, Macular)	38.2% (Nose, Trunk, Face)
Maculopapular Eruption	25.40%	53.50%	26.90%	33.90%
Oral Ulcers	25.40%	9.80%	ND	13.58%
Erythema of Pinna	6.01%	ND	ND	8.48%
Lichenoid Eruption	16.40%	ND	ND	2.46%
Exacerbation of Dermatoses	Psoriasis and Acne form Eruption	Psoriasis, Stasis Eczema	Psoriasis Lichen Planus	Psoriasis, Hansesn Type 1 Reaction, Stasis Dermatitis
CHIK IgM ab +VE	59.70%	55.30%	100%	97%

ND: Not described, CHIK IgM ab: Chikungunya viral serology.

Figure-2: Hyperpigmentation at nose, chick sign.

most common pattern of hyperpigmentation were patches at malar area of face, neck, trunk, back, dorsal aspects of limbs, palmar creases, ankle joint and oral cavity (Figure-1).

The second most common manifestation was erythematous maculopapular exanthem seen in 17(25.4%) patients. Generalised body ache 14(20%), malaise 23(35%) and tenderness of wrist and feet 7(10%) were observed in patients who presented with maculopapular rash. Oral ulcers were also documented as common mucocutaneous manifestation 17(25.4%); 5(7.4%) being of apthous type. The next most common cutaneous finding was diffuse hair-fall 14(20.9%). Lichenoid eruption was seen in 11(16.4%) cases. Flare up of pre-existing psoriasis, acne form eruptions, erythema of pinna, generalised urticarial eruptions were other prevalent findings (Table-1).

Discussion

CF is a viral disease characterised by sudden onset of fever associated with severe joint pain followed by constitutional symptoms and skin rashes.[3] All joints get involved at the same time, the condition gets more painful with fever which usually subsides by taking pain-killers. CF manifests itself after bite of infected mosquito with an incubation period of 3-12 days.[4]

In humans, Chikungunya virus manifests in about 48h after the mosquito bite, followed by blood high viraemia within 2 days.[7] Viraemia decreases in 3-5 days followed by the presence of haemagglutination inhibition (HI) and neutralising antibodies (NAs). Serum IgM antibody is detectable from day 5 after the onset of symptoms and remains persistent for 2-6 months.[7] Virus isolation could be possible during the period of viraemia (2-10 days) by inoculation of serum on vero or mosquito cells identification by immunofluorescence.[8,9] Reverse transcription-polymerase chain reaction (RT-PCR) using primer pairs is used to obtain result in 2 days. It is used to amplify several Chikungunya virus-specific genes from whole blood, generating millions of copies of genes in order to identify them. CF originated in Africa and now has affected the entire world.[9]

Postponement in diagnosis and treatment of diseases caused by these viruses can result in major patient morbidity and mortality.[10] CF may be seen in all age groups and both genders. In comparison to other countries in Asia, the current study showed female predominance in gender.[11,12]

Multiple CF epidemics were documented in Karachi.[13] The current study documented two main groups of mucocutaneous features of CF. One group, which presented with mucocutaneous manifestations within 1 month of onset of fever, was categorised as having early features of maculopapular rashes, oral ulcers, erythema of pinna, and exacerbation of psoriasis. The second group, which presented after 1 month of the onset of fever, was categorised as having late features, like patchy hyperpigmentation, lichenoid eruptions, diffuse hair-fall and exacerbation of acne.

Pattern of pigmentation included melasma type at malar area, lichened type at dorsal aspects of hands, feet, flexures, and back of neck and at palmar creases. Wood's lamp examinations showed mixed epidermal and dermal pattern of hyperpigmentation.

The characteristics of hyperpigmentation was diffuse, epidermal non-pruritic and non-inflammatory. They were not associated with postural hypotension, history of drug, gingival and oral pigmentation. Pathogenesis of pigmentation includes dispersion or retention of intra epidermal melanin caused by virus and post-inflammatory hyperpigmentation.[1] Studies showed similar pattern of pigmentation.[1,14] One study showed diffuse pattern of hyperpigmentation on body, which is a finding in contrast to the current study.[15]

One of the striking features noted in the current study was localised type of hyperpigmentation in centrofacial pattern mainly involving the nose (Figure-2). It is one of the most common cutaneous manifestations in acute phase of the disease and helps in the retrospective diagnosis of CF infection.[5,1,14]

The second most common manifestations noted were

maculopapular rashes. Skin manifestations have been reported in 55% patients during the first week by a study[16] which spared the face and involved mainly the trunk and limbs with islands of normal skin. In the current study, maculopapular rash presented mainly affecting the face, trunk and limbs with island of normal skin. It developed abruptly after the first 2-4 days of fever and subsided within a week without any significant sequel. Mild itching was present in 80% patients with rashes and it subsided by antihistamine and soothing lotions. In the current study, maculopapular eruption generally involved the whole body, but 3% patients also presented with localised erythema involving ear, nose, face and palate. Inamdar et al. also reported transient nasal erythema.[2] Kanan et al.[17] also reported pruritus in 80.8% patients, whereas it was present in 50% of patients in the current study. No abnormalities of bleeding time or clotting time were observed in our patients. Other viral causes were excluded.

Multiple painful aphthae-like ulcers in the oral cavity were documented as the third most common finding. It was present at the tip of the tongue, on gingival surface, and mucosal surface of the cheek. It was about 0.1-0.5cm, tender and had irregular margins. Some had erythematous borders with yellow base. Tzank smears were negative for acantholytic disorder. Culture was negative for bacterial and fungal infection. It usually appeared on day 3-5 after fever and subsided within a week of presentation without scarring. Patients were treated symptomatically. Ramesh et al. also notified apthous-like ulcer in patients affected with CF,[1] mostly affecting oral cavity.

Another common finding was hair-fall as a late cutaneous manifestation. Most of cases reported 2-3 months after fever and rashes. Other causes of hair-fall were excluded, like diffuse alopecia, Vitamin D3 deficiency, anaemia, thyroid disorders, history of any medicines, like contraceptive pills, anticoagulants, and anticonvulsant, telogen effluvium, tinea capitis, and other inflammatory conditions of hair-fall. Amin et al. showed similar pattern of hair-fall during and after a CF episode.[18]

Many patients developed lichenoid eruption after 6 months, but reported mostly after 1-1.5 years. They mostly presented with photo-exposed area, including back of neck, dorsal limb of both upper and lower limbs, face and trunk. It was characterised by the formation of hyperpigmented lichenified plaque scattered at multiple sites of body with irregular margins and violaceous hue. Some of them were pruritic. Skin biopsy excluded lichen planus and other lichenoid disorders. They were treated symptomatically. Riyaz et al.[14] also notified lichenoid eruption as a late CF manifestation.

Another important finding in the current study was typical erythema of ear pinna. Similar finding were observed by Ramesh et al.[1] describing pinna with erythema and swelling of the pinnae mimicking the Milian's ear sign of erysipelas. It is an acute manifestation which subsides within 10 days and is treated symptomatically.

Exacerbation of existing dermatoses has been well documented in CF. Few patients reported with exacerbation of psoriasis who were already on treatment for psoriasis without any history of provoking factors, like withdrawal of steroid, hypocalcaemia, electrolyte disturbance, sore throat. We noted increased Psoriasis Area and Severity Index (PASI) score after being affected by CF despite the treatment. Exacerbation of pre-existing acne on face was also documented that was polymorphic and with no other provoking and causative factors except history of CF. Inamdar et al.[2] and others showed different chronic inflammatory skin diseases exacerbation.[3,8,11]

The effect of Chikungunya on health of humans has immensely increased over the past two decades because the virus has the capability to evolve and has increased transmission ability.[19]

Various studies had explored CF and its manifestations in Pakistan,[20] but no single study was done on its important cutaneous aspects which was done in the current study. Global warming is one of the leading causes behind the range of movement of mosquitoes. Current decades have experienced a major change with the emergence of new viral infections worldwide.[21] The first reported outbreak of Chikungunya in Pakistan was from 2016 and since then many cases have been reported both in Pakistan and across the region[22-24] (Table-2).

The current study has limitations as it failed to determine the actual burden of CF with cutaneous findings because most of the patients did not consult any doctor in this regard. Further studies are required to prevent the patients against long term sequel of CF.

Conclusion

CF presented with unusual mucocutaneous findings, some of which remained present months or even years after the onset of CF. Cutaneous manifestations are usually ignored by most patients. While having late onset of presentation and its persistent nature, it is important to recognise them early for better outcome.

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